DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/17/10 has been entered.

Claims 1-7 have been cancelled. Claims 18 and 19 are new. Claims 8-19 are pending and under examination.

Withdrawn rejections:

Applicant's amendments and arguments filed 5/17/10 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below is herein withdrawn. Claim 8 was rejected under 35 U.S.C. 102(b) as being anticipated by Leslie et al. GB 2307857. Applicant amended the claim to recite that the active substance is not dispersed in the matrix. The rejection is withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 8 and 11 introduces new matter as the claim recites the limitation: "ingredient comprises at least 30% by weight of said first blend". There is no support in the specification for this limitation. The limitation of: "ingredient comprises at least 30% by weight of said first blend" was not described in the specification as filed, and person skilled in the art would not recognize in the applicant's disclosure a description of the invention as presently claimed. There is no guidance in the specification to select "ingredient comprises at least 30% by weight of said first blend" and from MPEP 2163.06: "Applicant should therefore specifically point out the support for any amendments made to the disclosure." Applicant has directed the Examiner to the examples in the specification for the amendments. However, the instant claim language includes all amounts greater than 30% and there is no support for that range. Example 1 only has 60% mannitol and example 3 has 30% mannitol but the claim language includes amounts such as 95%. Therefore, it is the Examiner's position

that the disclosure does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of filing of the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 8 and 11 recite: "said ingredient comprises at least 30% by weight of said first blend". Applicant's terminology has created an indefiniteness problem. An 'ingredient' reads on a single species such as a sugar alcohol and as such a single species is limited to that species and cannot comprise a combination of different ingredients which is the 'blend'. In contrast, a 'blend' may comprise multiple ingredients. Thus it is unclear how an 'ingredient' can comprise 'a blend' which is comprised of multiple ingredients. In the interest of compact prosecution, the claims will be examined as they read on at least 30% of the 'first blend' which is the 'at least one ingredient' and the effervescent system. Claims 9, 10 and 12-19 are rejected as being indefinite because they are dependent on an indefinite base claim. Correction is required.

Claim Rejections - 35 USC § 102

Claim Rejections - 35 USC § 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by Hoff et al. US 3872227 or in the alternative is rejected under 35 U.S.C. 103(a) as being unpatentable over Hoff et al. US 3872227.

Hoff et al. disclose formulations for oral administration (Abstract and claims 1-20). Hoff et al. disclose an effervescent tablet in Example 7:

EXAMPLE 7 — Phenoxymethylpenicillin Effervescent Tablets, 600,000 U each

32 parts of citric acid, 38 parts of sodium bicarbonate, 4.1 parts of sugar, 16 parts of glycine and 1.6 parts of serine are mixed and finely powdered by means of a mill. This mixture is subsequently uniformly moistened, in a kneader, with an alcoholic solution of 0.2 parts of sodium saccharin and dried in a fluidized bed.

The sieved granules are mixed with 7.1 parts of phenoxymethylpenicillin (either as the acid, or employed as the potassium salt, corresponding to 7.8 parts), 0.5 parts of tutti-frutti dry flavoring and 0.5 parts of sodium benzoate.

Effervescent tablets weighing 5.0 g each are prepared from this mixture and when dissolved in water give an aromatic, pleasant-tasting phenoxymethylpenicillin solution.

As is clearly disclosed by Hoff et al., an acidic component (citric acid), a CO2 donor (sodium bicarbonate), sugar (fusible sugar), and sugar substitute (sodium saccharin) are mixed and finely powdered to produce effervescent tablets. Hoff et al. teach using maltose, mannitol, and sorbitol in the composition (column 2, lines 32-36 and column 3, lines 19-25). In the absence of evidence to the contrary, the 'at least one ingredient' is present in an amount sufficient to stabilize at least one of the CO2 donor and acidic component and since the ingredients are mixed then it is the position of the Examiner that the CO2 donor and acidic component are dispersed throughout the substrate. Furthermore, the phenoxymethylpenicillin is inherently degradable in the absence of evidence to the contrary. Before being added to the effervescent system, the phenoxymethylpenicillin is not dispersed in the first blend of ingredient and carbon dioxide generator and is later mixed with the blend. The first blend of effervescent

system and ingredient comprises at least 30% by weight since there is 32 parts citric acid and 38 parts of sodium bicarbonate and 4.1 parts sugar.

With regards to the limitation of "a structure formed by melting said ingredient…", it is the position of the Examiner that this reads on a product by process. Please note that in product-by-process claims, "once a product appearing to be substantially identical is found and a 35 U.S.C. 102/103 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113. This rejection under 35 U.S.C. 102/103 is proper because the "patentability of a product does not depend on its method of production." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). In addition, please note that the Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether Applicants' stabilized medicament differs and, if so, to what extent, from that of the discussed reference.

Response to arguments:

Applicant asserts that the products are structurally different and argues that in Hoff, the method would leave "large numbers of effervescent crystals exposed on the surface of the resulting granules" whereas the instantly claimed structure requires the sugar to be melted thereby losing its crystal orientation and the effervescent material is dispersed in the sugar. While the Examiner appreciates the analogy set forth by Applicant it is merely conjecture without objective evidence.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 8-10, 16 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Robinson et al. US 6071539.

Robinson et al. disclose effervescent granules and thermal heat methods of preparing them comprising an acidic agent, a **hot-melt** extrudable binder capable of forming a eutectic mixture (solid solution) with the acidic agent and active agents (Abstract; tables 1-4; column 13, lines 43-45) and claims 1-16). As can be clearly seen in Table 4 below (with Examiner added emphasis),

TABLE 4

Drug-Containing Hot-Melt Extruded Effervescent Formulations

Ibuprofen	50	50	0	0	0	30
Chlorphesiamine Maleate	0	0	5	5	0	5
Pseudoephridine HCl	0	0	0	25	20	
AcDiSol	5	5	0	0	5	5
Microcrystalline Cellulose	20	10	32	20		5
Na Bicarbonate	13	13	15	18	20	15
Citric Acid	12	12	14	15	18	13
PEG 3350	0	10	14	12	10	12
Crosslinked PVP	0	0	5	3	3	3
Explotab	0	0	0	2		2
Mannitol	0	0	5		9	
Xylitol	0	0	10		15	10

formulations with an acidic component (citric acid), a CO2 donor (bicarbonate), a pharmaceutically active substance (ibuprofen) and at least one ingredient that is a sugar alcohol (xylitol). In one example, there is 10% xylitol, 13% citric acid and 15% Na bicarbonate to make a 'blend' of greater than 30%. The Examiner notes that Applicant discloses xylitol as a preferred sugar alcohol for use in the invention (page 4, lines 10-11 of the instant specification) which would inherently have the melting points claimed by Applicant. *Robinson teaches using binders, such as sugars up to about 60% of the total composition* (column 5, lines 33-45). Furthermore, Robinson teaches in Table 3 formulation H which is a composition with 28% mannitol and 5% aspartame (sugar substitute) which provides greater than 30% of 'the ingredient'. Water is not present in Table 3 or 4. Additionally, ***47% lactose*** is used in Granule C (column 19) and ***62% mannitol*** is used in Granule G (column 20). The mixtures are taught by Robinson et al. to be **hot melt extruded blended mixtures** which would inherently read on a structure

formed by melting the substrate and re-solidifying the substrate that has the acidic ingredient substantially dispersed throughout the substrate and a substrate that has the ingredient as a substantial constituent. Therefore, instant claims 8-10 are anticipated. Robinson et al. teach a composition with *aspirin*, mannitol, an acidic component stearic acid, effervescent granule EG (B) which has sodium bicarbonate, and aspartame which reads on a composition with a CO2 donor, acid component, a degradable pharmaceutical active ingredient and at least one ingredient selected from sugars and sugar substitutes (column 16, lines 19-24 and column 19, lines 57-65):

E.

Ingredients	Amount (% Wt.)
Aspirin	50
Mannitol	15
AVICEL PH101	25.5
Aspartame	1.5
Stearic Acid	2.0
EG (B)	5.0

.

Thus, instant claim 16 is anticipated.

The temperature of the hot melt extrusion will not exceed 150 C which reads on instant claims 12 and 13 (column 14, lines 1-5). Tablets are disclosed which reads on instant claim 15 (examples 3-9, for example). The rate of effervescence can be controlled by varying the hot-melt extrudable binder which can be xylitol or by the relative amounts of ingredients (column 6, line 32-column 7, line 23). Robinson et al. teach grinding the dried granulation which reads on comminution after cooling of instant claim 14 (column 22, lines 24-26).

With regards to the limitation of "a structure formed by melting said ingredient…", it is the position of the Examiner that this reads on a product by process. Please note

that in product-by-process claims, "once a product appearing to be substantially identical is found and a 35 U.S.C. 102 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113. This rejection under 35 U.S.C. 102 is proper because the "patentability of a product does not depend on its method of production." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). In addition, please note that the Patent and Trademark Office is not equipped to conduct experimentation in order to determine whether Applicants' stabilized medicament differs and, if so, to what extent, from that of the discussed reference.

Response to arguments:

Applicant argues that the claim amendments require that the active is not incorporated into the melted material and that Robinson is not concerned with the long term stability of the active ingredient. These arguments are not persuasive because: "patentability of a product does not depend on its method of production." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). Furthermore, the Examiner notes that at some point the active must be added to the 'blend' and applicant teaches mixing the 'blend' with the active (See instant specification examples 1-3, for example). Therefore, the active is dispersed in the 'blend' to make the final product. These arguments are not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 11-15, 17 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robinson et al. (US 6071539).

Applicant claims:

11(Currently Amended). A process for producing a stabilized medicament, said stabilized medicament comprising:

(A) an effervescent system comprising:

(i) a CO_2 donor, and

(ii) an acidic component;

(B) a ~~degradable~~ pharmaceutically active substance, and

(C) at least one ingredient selected from the group consisting of fusible sugars, sugar alcohols, and sugar substitutes,

wherein said process comprises the steps of: (a) at least partially melting said ingredient, (b) mixing at least one of said CO_2 donor and said acidic component with said at least partially melted ingredient to form an at least partially molten blend in which said at least one of said CO_2 donor and said acidic component is dispersed, (c) cooling said at least partially molten blend to form a first blend, (d) combining said cooled at least partially molten blend, said pharmaceutically active substance and any remaining portion of said effervescent system and (e) forming said stabilized medicament, wherein said ~~ingredient is present in an amount sufficient to stabilize at least one of said CO_2 donor, said acidic component, and said degradable pharmaceutically active substance~~ ingredient comprises at least 30% by weight of said first blend and said degradable pharmaceutically active substance is not dispersed in said first blend.

Determination of the scope and content of the prior art

(MPEP 2141.01)

The reference of Robinson et al. is discussed in detail above and that discussion is hereby incorporated by reference.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. The difference between the instant application and Robinson et al. is that Robinson et al. do not expressly teach the order of steps (a)-(e) where the active substance is not dispersed in the 'blend' as instantly claimed.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to perform the method of Robinson by performing steps (a)-(e) where the active substance is not dispersed in the 'blend' of instant claim 11, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because: 1) selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results. (*In re Burhans*, 154 F.2d 690, 69 USPQ 330 (CCPA

1946) (); and 2) Selection of any order of mixing ingredients is prima facie obvious. (*In re Gibson*, 39 F.2d 975, 5 USPQ 230 (CCPA 1930)).

Robinson et al. mixes the components and then hot-melts them while Applicant merely melts one component first and then adds others to the first component. At some point the active must be added to the 'blend' as taught by Applicant in at least examples 1-3. All Applicant has done is pre-mix the 'blend' and then added the active substance which is then intrinsically dispersed in the 'blend'. This is simply changing the order of mixing ingredients. No unexpected results have been argued.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to arguments:

Applicant asserts that Robinson does not teach the amount of xylitol instantly claimed. However, the claims do not recite a specific percentage of xylitol as discussed in the 112 second paragraph rejection above and Robinsion teaches using greater than 30% sugars as discussed above. These arguments are not persuasive and the rejection is maintained.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (7:15 am-4:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ernst V Arnold/

Primary Examiner, Art Unit 1616